

WHAT IS CLAIMED IS:

1. An isolated and purified DNA molecule which encodes a bradykinin B₁ receptor or a functional derivative thereof.

5 2. The isolated and purified DNA molecule of claim 1, having a nucleotide sequence:

CAGAGAAAACCTCCTCCAAAAGCAGCTCTCACTATCAGAAAACCCAACTAC
AGTTGTGAACGCCTTCATTTTCTGCCTGAGGTCTCAGTCCGTCGGCCCAG
ACTGAAGTGCAGTGGCACAATCATAGCTCGCTGCAGCCTCGACCTTCCAG
10 GCTTAAACGATTCTCCCACCTCAGCCTCTCGAGTTGCTGGGACCACAGGT
CACTGTGCATGGCATCATCCTGGCCCCCTCTAGAGCTCCAATCCTCCAAC
CAGAGCCAGCTCTTCCCTCAAAATGCTACGGCCTGTGACAATGCTCCAGA
AGCCTGGGACCTGCTGCACAGAGTGCTGCCGACATTTATCATCTCCATCT
GTTTCTTCGGCCTCCTAGGGAACCTTTTTTGTCTGTTGGTCTTCCTCCTG
15 CCCCCGGCGGCAACTGAACGTGGCAGAAATCTACCTGGCCAACCTGGCAGC
CTCTGATCTGGTGTTTGTCTTGGGCTTGCCCTTCTGGGCAGAGAATATCT
GGAACCAGTTTAACTGGCCTTTCGGAGCCCTCCTCTGCCGTGTCATCAAC
GGGGTCATCAAGGCCAATTTGTTTCATCAGCATCTTCCTGGTGGTGGCCAT
CAGCCAGGACCGCTACCGCGTGCTGGTGCACCCTATGGCCAGCGGAAGGC
AGCAGCGGCGGAGGCAGGCCCGGGTCACCTGCGTGCTCATCTGGGTGTG
20 GGGGGCCTCTTGAGCATCCCCACATTCCTGCTGCGATCCATCCAAGCCGT
CCCAGATCTGAACATCACCGCCTGCATCCTGCTCCTCCCCCATGAGGCCT
GGCACTTTGCAAGGATTGTGGAGTTAAATATTCTGGGTTTCCTCCTACCA
CTGGCTGCGATCGTCTTCTTCAACTACCACATCCTGGCCTCCCTGCGAAC
GCGGGAGGAGGTCAGCAGGACAAGGTGCGGGGGCCGCAAGGATAGCAAGA
25 CCACAGCGCTGATCCTCACGCTCGTGGTTGCCTTCCTGGTCTGCTGGGCC
CCTTACCACTTCTTTGCCTTCCTGGAATTCTTATTCCAGGTGCAAGCAGT
CCGAGGCTGCTTTTGGGAGGACTTCATTGACCTGGGCCTGCAATTGGCCA
ACTTCTTTGCCTTCACTAACAGCTCCCTGAATCCAGTAATTTATGTCTTT
GTGGGCCGGCTCTTCAGGACCAAGGTCTGGGAACCTTTATAACAATGCAC
30 CCCTAAAAGTCTTGCTCCAATATCTTCATCCCATAGGAAAGAAATCTTCC
AACTTTTCTGGCGGAATTAAAACAGCATTTGAACCAAGAAAAAAAAAAAAA
AAAAAA (SEQ.ID.NO.:1) or functional derivatives thereof.

3. The isolated and purified DNA molecule of claim 1, wherein said DNA molecule is genomic DNA.

4. An expression vector for expression of a bradykinin B₁ receptor in a recombinant host, wherein said vector contains a recombinant gene encoding a bradykinin B₁ receptor or functional derivative thereof.

5. The expression vector of claim 4, wherein the expression vector contains a cloned gene encoding the bradykinin B₁ receptor, having a nucleotide sequence:

CAGAGAAAACCTCCTCCAAAAGCAGCTCTCACTATCAGAAAACCCAACTAC
AGTTGTGAACGCCTTCATTTTCTGCCTGAGGTCTCAGTCCGTCGGCCCAG
ACTGAAGTGCAGTGGCACAATCATAGCTCGCTGCAGCCTCGACCTTCCAG
GCTTAAACGATTCTCCACCTCAGCCTCTCGAGTTGCTGGGACCACAGGT
CACTGTGCATGGCATCATCCTGGCCCCCTCTAGAGCTCCAATCCTCCAAC
CAGAGCCAGCTCTTCCCTCAAATGCTACGGCCTGTGACAATGCTCCAGA
AGCCTGGGACCTGCTGCACAGAGTGCTGCCGACATTTATCATCTCCATCT
GTTTCTTCGGCCTCCTAGGGAACCTTTTTGTCTGTTGGTCTTCCTCCTG
CCCCGGCGGCAACTGAACGTGGCAGAAATCTACCTGGCCAACCTGGCAGC
CTCTGATCTGGTGTGTTGTCTTGGGCTTGCCCTTCTGGGCAGAGAATATCT
GGAACCAGTTTAACTGGCCTTTCGGAGCCCTCCTCTGCCGTGTCATCAAC
GGGGTCATCAAGGCCAATTTGTTTCATCAGCATCTTCCTGGTGGTGGCCAT
CAGCCAGGACCGCTACCGCGTGCTGGTGCACCTATGGCCAGCGGAAGGC
AGCAGCGGCGGAGGCAGGCCCCGGGTACCTGCGTGCTCATCTGGGTGTG
GGGGGCCTCTTGAGCATCCCCACATTCTGCTGCGATCCATCCAAGCCGT
CCCAGATCTGAACATCACCGCCTGCATCCTGCTCCTCCCCCATGAGGCCT
GGCACTTTGCAAGGATTGTGGAGTTAAATATTCTGGGTTTCCTCCTACCA
CTGGCTGCGATCGTCTTCTTCAACTACCACATCCTGGCCTCCCTGCGAAC
GCGGGAGGAGGTGAGCAGGACAAGGTGCGGGGGCCGCAAGGATAGCAAGA
CCACAGCGCTGATCCTCACGCTCGTGGTTGCCTTCCTGGTCTGCTGGGCC
CCTTACCACTTCTTTGCCTTCTGGAATTCTTATTCCAGGTGCAAGCAGT
CCGAGGCTGCTTTTGGGAGGACTTCATTGACCTGGGCCTGCAATTGGCCA
ACTTCTTTGCCTTCACTAACAGCTCCCTGAATCCAGTAATTTATGTCTTT
GTGGGCGCGCTCTTCAGGACCAAGGTCTGGGAACCTTTATAACAATGCAC
CCCTAAAAGTCTTGCTCCAATATCTTCATCCCATAGGAAAGAAATCTTCC

AACTTTTCTGGCGGAATTAAAACAGCATTGAACCAAGAAAAAAAAAAAAA
AAAAAA (SEQ.ID.NO.:1) or functional derivative thereof.

5 6. The expression vector of claim 4, wherein the
expression vector contains genomic DNA encoding the bradykinin B1
receptor.

10 7. A recombinant host cell containing a
recombinantly cloned gene encoding a bradykinin B1 receptor or
functional derivative thereof.

8. The recombinant host cell of claim 7, wherein said
gene encoding the bradykinin B1 receptor has a nucleotide sequence:
15 CAGAGAAAACCTCCTCCAAAAGCAGCTCTCACTATCAGAAAACCCAACTAC
AGTTGTGAACGCCTTCATTTTCTGCCTGAGGTCTCAGTCCGTCCGCCAG
ACTGAAGTGCAGTGGCACAATCATAGCTCGCTGCAGCCTCGACCTTCCAG
GCTTAAACGATTCTCCACCTCAGCCTCTCGAGTTGCTGGGACCACAGGT
CACTGTGCATGGCATCATCCTGGCCCCCTCTAGAGCTCCAATCCTCCAAC
CAGAGCCAGCTCTTCCCTCAAATGCTACGGCCTGTGACAATGCTCCAGA
AGCCTGGGACCTGCTGCACAGAGTGCTGCCGACATTTATCATCTCCATCT
20 GTTTCTTCGGCCTCCTAGGGAACCTTTTTGTCTGTTGGTCTTCCTCCTG
CCCCGGCGGCAACTGAACGTGGCAGAAATCTACCTGGCCAACCTGGCAGC
CTCTGATCTGGTGTGTTGTCTTGGGCTTGCCCTTCTGGGCAGAGAATATCT
GGAACCAGTTTAACTGGCCTTTCGGAGCCCTCCTCTGCCGTGTCATCAAC
GGGGTCATCAAGGCCAATTTGTTCATCAGCATCTTCCTGGTGGTGGCCAT
25 CAGCCAGGACCGCTACCGCGTGCTGGTGCACCCTATGGCCAGCGGAAGGC
AGCAGCGGCGGAGGCAGGCCCCGGGTCACCTGCGTGCTCATCTGGGTTGTG
GGGGGCCTCTTGAGCATCCCCACATTCCTGCTGCGATCCATCCAAGCCGT
CCCAGATCTGAACATCACCGCCTGCATCCTGCTCCTCCCCCATGAGGCCT
GGCACTTTGCAAGGATTGTGGAGTTAAATATTCTGGGTTTCCTCCTACCA
CTGGCTGCGATCGTCTTCTTCAACTACCACATCCTGGCCTCCCTGCGAAC
30 GCGGGAGGAGGTCAGCAGGACAAGGTGCGGGGGCCGCAAGGATAGCAAGA
CCACAGCGCTGATCCTCACGCTCGTGGTTGCCTTCCTGGTCTGCTGGGCC
CCTTACCACTTCTTTGCCTTCCTGGAATTCTTATTCCAGGTGCAAGCAGT
CCGAGGCTGCTTTTGGGAGGACTTCATTGACCTGGGCCTGCAATTGGCCA
ACTTCTTTGCCTTCACTAACAGCTCCCTGAATCCAGTAATTTATGTCTTT

GTGGGCCCGGCTCTTCAGGACCAAGGTCTGGGAACCTTTATAACAATGCAC
CCCTAAAAGTCTTGCTCCAATATCTTCATCCCATAGGAAAGAAATCTTCC
AACTTTTCTGGCGGAATTAAAACAGCATTGAACCAAGAAAAAAAAAAAAA
AAAAAA (SEQ.ID.NO.:1) or functional derivative thereof.

5 9. The recombinant host cell of claim 7, wherein said
cloned gene encoding the bradykinin B₁ receptor is genomic DNA.

10 10. A protein, in substantially pure form which
functions as a bradykinin B₁ receptor.

11. The protein according to claim 10, having an amino
acid sequence:

Met Ala Ser Ser Trp Pro Pro Leu Glu Leu Gln Ser Ser Asn
Gln Ser Gln Leu Phe Pro Gln Asn Ala Thr Ala Cys Asp Asn
15 Ala Pro Glu Ala Trp Asp Leu Leu His Arg Val Leu Pro Thr
Phe Ile Ile Ser Ile Cys Phe Phe Gly Leu Leu Gly Asn Leu
Phe Val Leu Leu Val Phe Leu Leu Pro Arg Arg Gln Leu Asn
Val Ala Glu Ile Tyr Leu Ala Asn Leu Ala Ala Ser Asp Leu
Val Phe Val Leu Gly Leu Pro Phe Trp Ala Glu Asn Ile Trp
20 Asn Gln Phe Asn Trp Pro Phe Gly Ala Leu Leu Cys Arg Val
Ile Asn Gly Val Ile Lys Ala Asn Leu Phe Ile Ser Ile Phe
Leu Val Val Ala Ile Ser Gln Asp Arg Tyr Arg Val Leu Val
His Pro MET Ala Ser Gly Arg Gln Gln Arg Arg Arg Gln Ala
Arg Val Thr Cys Val Leu Ile Trp Val Val Gly Gly Leu Leu
25 Ser Ile Pro Thr Phe Leu Leu Arg Ser Ile Gln Ala Val Pro
Asp Leu Asn Ile Thr Ala Cys Ile Leu Leu Leu Pro His Glu
Ala Trp His Phe Ala Arg Ile Val Glu Leu Asn Ile Leu Gly
Phe Leu Leu Pro Leu Ala Ala Ile Val Phe Phe Asn Tyr His
Ile Leu Ala Ser Leu Arg Thr Arg Glu Glu Val Ser Arg Thr
30 Arg Cys Gly Gly Arg Lys Asp Ser Lys Thr Thr Ala Leu Ile
Leu Thr Leu Val Val Ala Phe Leu Val Cys Trp Ala Pro Tyr
His Phe Phe Ala Phe Leu Glu Phe Leu Phe Gln Val Gln Ala
Val Arg Gly Cys Phe Trp Glu Asp Phe Ile Asp Leu Gly Leu
Gln Leu Ala Asn Phe Phe Ala Phe Thr Asn Ser Ser Leu Asn

Pro Val Ile Tyr Val Phe Val Gly Arg Leu Phe Arg Thr Lys
Val Trp Glu Leu Tyr Lys Gln Cys Thr Pro Lys Ser Leu Ala
Pro Ile Ser Ser Ser His Arg Lys Glu Ile Phe Gln Leu Phe
Trp Arg Asn (SEQ.ID.NO.:2) or functional derivative thereof

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12. A monospecific antibody immunologically reactive
with a bradykinin B₁ receptor.

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13. The antibody of Claim 12, wherein the antibody
blocks activity of the bradykinin B₁ receptor.

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14. A process for expression of a bradykinin B₁
receptor protein in a recombinant host cell, comprising:
(a) transferring the expression vector of Claim 4
into suitable host cells; and
(b) culturing the host cells of step (a) under
conditions which allow expression of the
bradykinin B₁ receptor protein from the
expression vector.

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15. A method of identifying compounds that modulate
bradykinin B₁ receptor activity, comprising:

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- (a) combining a suspected modulator of
bradykinin B₁ receptor activity with a
bradykinin B₁ receptor; and
- (b) measuring an effect of the modulator on the
receptor.

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16. The method of claim 15, wherein the effect of the
modulator on the receptor is inhibiting or enhancing binding of B₁
receptor ligands.

17. The method of claim 15, wherein the effect of the modulator on the receptor is stimulation or inhibition of signal transduction mediated by B₁ receptors.

5 18. The method of claim 17, wherein the effect of the modulator on the receptor is signal transduction mediated by B₁ receptors, and said signal transduction is selected from the group consisting of phosphatidyl inositol hydrolysis, release of intracellular Ca²⁺ stores, and arachidonic acid release.

10 19. A compound active in the method of Claim 15, wherein said compound is a modulator of a bradykinin B₁ receptor.

15 20. A compound active in the method of Claim 15, wherein said compound is an agonist or antagonist of a bradykinin B₁ receptor.

20 21. A compound active in the method of Claim 15, wherein said compound is a modulator of expression of a bradykinin B₁ receptor.

22. A pharmaceutical composition comprising a compound active in the method of Claim 15, wherein said compound is a modulator of bradykinin B₁ receptor activity.

25 23. A method of treating a patient in need of such treatment for a condition which is mediated by a bradykinin B₁ receptor, comprising administration of a bradykinin B₁ receptor modulating compound active in the method of Claim 15.

30 24. A method of treating a patient in need of such treatment for a condition which is mediated by a bradykinin B₁ receptor and is characterized by hyperalgesia, acute inflammation or

chronic inflammation, comprising administration of a bradykinin B₁ receptor modulating compound active in the method of Claim 15.

25. A method of identifying compounds that modulate bradykinin B₁ receptor activity, comprising:

- (a) combining a suspected modulator of bradykinin B₁ receptor activity with a cell expressing a recombinant bradykinin B₁ receptor; and
- (b) measuring an effect of the modulator on the receptor.

26. The method of claim 25, wherein the effect of the modulator on the receptor in step (b) is inhibiting or enhancing binding of B₁ receptor ligands.

27. The method of claim 25, wherein the effect of the modulator on the receptor in step (b) is inhibition or enhancement of signal transduction mediated by B₁ receptors.

28. The method of claim 27, wherein the signal transduction is selected from a group consisting of phosphatidyl inositol hydrolysis, release of intracellular Ca²⁺ stores, and arachidonic acid release.

29. A compound active in the method of Claim 25, wherein said compound is a modulator of a bradykinin B₁ receptor.

30. A compound active in the method of Claim 25, wherein said compound is an agonist or antagonist of a bradykinin B₁ receptor.

31. A compound active in the method of Claim 25,
wherein said compound is a modulator of expression of a bradykinin
B₁ receptor.

5 32. A pharmaceutical composition comprising a
compound active in the method of Claim 25, wherein said compound
is a modulator of bradykinin B₁ receptor activity.

10 33. A method of treating a patient in need of such
treatment for a condition which is mediated by a bradykinin B₁
receptor, comprising administration of a bradykinin B₁ receptor
modulating compound active in the method of Claim 25.

15 34. A method of treating a patient in need of such
treatment for a condition which is mediated by a bradykinin B₁
receptor and is characterized by hyperalgesia, acute inflammation or
chronic inflammation, comprising administration of a bradykinin B₁
receptor modulating compound active in the method of Claim 25.

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